RESPONSE TO OFFICE ACTION

I. Status of the Claims

Claims 1–3 and 7–15 are pending in the application. Applicant elected to prosecute claims 1–3 and 7–15 in a Response to Restriction Requirement dated October 23, 2002. Claims 4–6 and 16–85 stand withdrawn as being drawn to a nonelected invention. Claims 1–3 and 7–15 stand rejected under 35 U.S.C. §112 second paragraph and 35 U.S.C. §112 first paragraph; claims 1, 7, 10–13 and 15 stand rejected under 35 U.S.C. §102(b) over Myers and Myers; and claims 1, 7, and 10–15 stand rejected under 35 U.S.C. §102(e) over Blaschuk. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1–3 and 7–15 stand rejected under 35 U.S.C. §112 second paragraph. The examiner states that the terms "peptide" and "drug" are unclear and indefinite because the intended peptide of claims 1 and 7 and the drug of claim 7 are not defined.

The proper test of definiteness is whether, in the light of the teachings of the prior art and of the particular application disclosure, the claims set out and circumscribe, for one possessing an ordinary level of skill in the pertinent art, a particular area with a reasonable degree of particularity. *In re Moore*, 169 U.S.P.Q. 236 (C.C.P.A. 1971). It is the function of the specification and not the claims to set forth operable parameters.

In the specification on page 18, lines 22 – 23 of the application, it is stated that the term "peptide" is defined as "a chain of up to about 50 amino acids." The peptides of the invention are further defined as having "the ability to be specifically uptaken by cancer/tumor cells and not by normal cells." (page 27, line 27).

Similarly, the application states that "[t]he term "drug" as used herein is defined as a medicament or medicine which is used for the therapeutic treatment of a medical condition or disease. The drug may be used in combination with another drug or type of therapy and in a preferred embodiment is effective for the treatment of cancer." (page 17, lines 15-18).

Therefore, both the term "peptide" and the term "drug" are clearly defined and definite. Particular peptides of the invention are described in the application and include the HN-1 peptide, as well as other variants and HN-1 related peptides that retain the ability to translocate through the tumor cell membranes. Similarly, particular drugs useful in the invention are described in the specification and in the claims and include doxorubicin, daunorubicin, mitomycin, actinomycin D, bleomycin, cisplatin, VP16, tumor necrosis factor, taxol, vincristine, vinblastine, carmustine, melphalan, cyclophosphamide, chlorambucil, busulfan, and lomustine.

The examiner also states that it is unclear whether the peptide or drug is effective and used for all types of tumors. The specification describes particular tumors and tumor types that can be treated with the various drugs described in the application. For example, the specification teaches that the drug doxorubicin is a first choice treatment for tumors associated with thyroid adenoma and primary hepatocellular carcinoma. Thirty-one other cancers for which doxorubicin has been found to be effective as a component of a first-choice combination are also provided (page 45, lines 10–17). Similarly, the application at page 20, lines 7-8 describes a specific embodiment where the HN-1 or HN-1 related peptides are "specifically internalized by the human head and neck squamous carcinoma cells or certain other solid tumor tissue cells, such as breast cancer cells."

Therefore, the specification provides a person possessing an ordinary level of skill in the art a reasonable degree of particularity to understand and practice the invention of claims 1–3 and 7–15. Therefore, applicants respectfully ask that the rejections under 35 U.S.C. §112 second paragraph be withdrawn.

III. Rejection Under 35 U.S.C. §112, First Paragraph

The examiner rejects claims 1–3 and 7–15 under 35 U.S.C. §112 first paragraph, stating that the specification, while being enabling for a peptide consisting of SEQ ID No: 1, does not reasonably provide enablement for any peptide that is capable of internalizing into a tumor cell. The examiner states that, since there is no mention of any other sequences or peptides other than that of SEQ ID NO:1 or the HN-1 peptide, one of skill in the art would not know where to begin the screening of a peptide that is capable of internalizing into a tumor cell and would be forced into undue experimentation to make and or practice the invention. The examiner further finds that, given the broad range of peptides and compositions encompassed within the claims, which includes proteins, antibody fragments, peptide conjugates, and small peptides, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Applicants respectfully traverse. The specification is enabling for a peptide and a composition comprising a peptide and a drug as claimed herein. Claims 1 and 7 have been amended to include the phrase "wherein said peptide comprises HN-1, a variant of HN-1, or a HN-1 related peptide" to more succinctly claim the invention.

This amendment does not introduce new matter and is supported by the specification. Specifically, on page 27, lines 26–27, the specification states that, in addition to HN-1, "[a]lso contemplated are other variants and HN-1 related peptides that still retain the ability to

translocate through the tumor cell membranes." Variants of HN-1 that are contemplated as part of the current invention are discussed, for example from page 23 to page 27 of the specification. HN-1 related peptides contemplated as part of the current invention are discussed, for example, on page 26, lines 19–22 of the specification where it states that the "substitution of amino acids to generate motifs that have stronger binding to tumor cells; or that can be specifically tailor-made to bind different types of tumor cells can allow the generation of more HN-1 related peptides, each different for a different tumor-type."

Example 2 shows the screening method used to obtain the peptide of SEQ ID NO:1. In addition, the application is enabling for the non-elected inventions that teach the screening of peptides that target tumor cells and are internalized by the tumor cell. Claim 78 as filed and the specification on page 13 gives a method for the isolation of an internalizing peptide with the steps of: (1) obtaining a peptide library; (2) individually contacting these peptides with members of a cell population; and (3) assaying for endocytosis of the peptides by the members of the cell population. Further claims describe the peptide library as a random peptide-display library or more particularly as a M13 single-stranded bacteriophage-based random peptide-display library. Applicants contend that it will not require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims as amended.

Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph be withdrawn.

IV. Rejection Under 35 U.S.C. §102(b)

A. Myer et al. (WO 88/00837) and Myer et al. (U.S. Pat. No. 5,087,616)

Claims 1, 7, 10-13, and 15 stand rejected under 35 U.S.C. §102(b) over Myer et al.(WO 88/00837) and Myer et al. (U.S. Pat. No. 5,087,616) (collectively referred to as Myer). The examiner states that Myer teach a peptide that is capable of internalizing into a tumor cell and further teach a composition comprising the peptide and a drug.

Myer teaches the use of a homing agent which should promote the internalization (receptor interaction) of the conjugate. This homing agent is attached to a polymeric carrier for a cytotoxic agent (pg. 8, col. 5). In particular, Myer describes Compound II, a pyrrolidinie-dione, which is attached to a drug molecule and a polymer and is described as being internalized by human squamous carcinoma cells. (pg. 18, col. 12).

Anticipation under §102(b) requires that each and every element of the claimed invention be described, either expressly or inherently, in a single prior art reference. *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316, 1327, 58 U.S.P.Q.2d 1545, 1552 (Fed. Cir. 2001); *Verdegaal Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987).

Because Myer does not teach a peptide comprising HN-1, a variant of HN-1, or a HN-1 related peptide, and the invention as amended claims only peptides comprising HN-1, a variant of HN-1, or a HN-1 related peptide, Myer does not teach or suggest every element of the present invention. As such, Meyer does not anticipate the rejected claims. Accordingly, Applicants respectfully request that the rejection to claims 1, 7, 10 – 13, and 15 under 35 U.S.C. §102(b) be withdrawn.

Applicants wish to clarify that the composition of claim 7 is not limited to a drug "selected from the group consisting of a chemotherapeutic agent, cytotoxic agent, apoptotic agent, DNA damaging agent, and chemotherapeutic agent" as suggested by the examiner but encompass all drugs as defined in the specification.

V. Rejection Under 35 U.S.C. §102(e)

B. Blaschuk (U.S. Patent 6,303,576)

The examiner rejects claims 1, 7, and 10–15 under 35 U.S.C. §102(e) over Blaschuk. The examiner states that Blaschuk teaches a peptide that is capable of internalizing into tumor cells, and a composition that comprises the peptide and a drug.

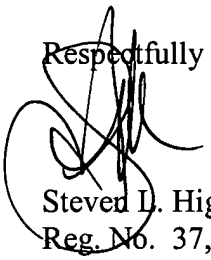
Blaschuk teaches a modulating agent linked to an internalization moiety such as a peptide, compound, liposome, or particle. The internalization moiety is used to improve the ability of an agent to penetrate the lipid bilayer of the cellular plasma membrane." (col. 9, lines 12–16). Blaschuk teaches the use of specific peptides as examples for an internalization moiety. However, he does not teach or suggest a peptide comprises HN-1, a variant of HN-1, or a HN-1 related peptide.

Applicants have amended the claims to make explicit that the claimed invention is directed to peptides which comprise HN-1, a variant of HN-1, or a HN-1 related peptide. Thus, it is believed that the claims as amended are not anticipated by Blaschuk. Reconsideration and withdrawal of the rejection to claims 1, 7, and 10–15 under 35 U.S.C. §102(e) is respectfully requested.

VI. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. The Examiner is invited to contact the undersigned agent at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Appendix A: Marked Up Copy of Amended Claims

1. (Amended) A peptide that targets a tumor cell, wherein said peptide comprises HN-1, a variant of HN-1, or a HN-1 related peptide and said peptide is internalized by said tumor cell.

7. (Amended) A composition comprising:

   a) a drug; and

   b) a peptide that targets a tumor cell, wherein said peptide comprises HN-1, a variant of HN-1, or a HN-1 related peptide and said peptide is internalized by said tumor cell

Appendix B: Clean Copy of Pending Claims After Entry of Amendments (Unofficial)

1. (Amended) A peptide that targets a tumor cell, wherein said peptide comprises HN-1, a variant of HN-1, or a HN-1 related peptide and said peptide is internalized by said tumor cell.

2. The peptide of claim 1, comprising SEQ ID NO:1.

3. The peptide of claim 1, consisting of SEQ ID NO:1.

7. (Amended) A composition comprising:
   a) a drug; and
   b) a peptide that targets a tumor cell, wherein said peptide comprises HN-1, a variant of HN-1, or a HN-1 related peptide and said peptide is internalized by said tumor cell.

8. The composition of claim 7, wherein said peptide comprises SEQ ID NO:1.

9. The composition of claim 7, wherein said peptide consists of SEQ ID NO:1.

10. The composition of claim 7, wherein said drug is a chemotherapeutic agent.

11. The composition of claim 7, wherein said drug is a cytotoxic agent.

12. The composition of claim 7, wherein said drug is an apoptotic agent.

13. The composition of claim 7, wherein said drug is a DNA-damaging agent.

14. The composition of claim 7, wherein said drug is Taxol.

15. The composition of claim 7, wherein said drug is cisplatin (CDDP), carboplatin, procarbazine, mechlorethamine, cyclophosphamide, ifosfamide, melphalan, chlorambucil, bisulfan, nitrosurea, dactinomycin, daunorubicin, doxorubicin, bleomycin, plicomycin, mitomycin, etoposide (VP16), tamoxifen, transplatinum, 5-fluorouracil, vincristin, vinblastin or methotrexate.